Annals of Clinical and Analytical Medicine
Case Report

Gaucher disease and SARS-CoV-2 infection: A case report

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Abstract
Gaucher disease is an autosomal recessive genetic disorder, caused by deficiency of the lysosomal enzyme, glucocerebrosidase, which leads to an accumulation of glucosylceramide in macrophages. It causes splenomegaly, hepatomegaly, cytopenia, and bone lesions associated with infiltration of bone marrow, spleen, and liver by Gaucher cells. A new coronavirus named severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) causing severe acute respiratory disease, emerged in China in December 2019. Most of the infected children appear to be asymptomatic or have a milder clinical course in contrast with adults. Herein, we report a pediatric case of Gaucher disease with SARS-CoV-2 infection.

Keywords
Gaucher, SARS-CoV-2, Enzyme Therapy

DOI: 10.4328/ACAM.21229 Received: 2022-05-15 Accepted: 2023-04-29 Published Online: 2023-08-08 Printed: 2023-09-25 Ann Clin Anal Med 2023;14(Suppl 2):S200-202
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Introduction

Gaucher disease (GD), the most common sphingolipidosis, is an autosomal recessive genetic disorder, caused by a deficiency of the lysosomal enzyme, glucocerebrosidase, which leads to an accumulation of glucosylceramide in macrophages [1].

Three clinical forms have been identified as type 1 (adult or non-neuronopathic type),which is the most common (95%) and typically causes no neurological damage [1].

Although most of the infected children with severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) appear to be asymptomatic or have a milder clinical course in contrast with infected adults [2], severe cases have been reported in children with underlying chronic diseases, comorbidity, immunosuppression, and in the younger pediatric age group [3]. Currently, there is no sufficient data if patients with GD have a higher risk of SARS-CoV-2 infection or whether it causes a more severe clinical course. A pediatric case of Gaucher disease with SARS-CoV-2 infection was presented in this report.

Case Report

An eleven-year-old boy has been followied with the diagnosis of GD type 1 in the department of pediatric gastroenterology since 2013. He received enzyme replacement treatment (ERT) (60 U/kg/2 weeks). In his routine follow-up, he had a cough and when questioned we learned that his mother had a SARS-CoV-2 infection.

In his physical examination, his weight was 24 kg (<3rd centile) and his height was 126 cm (3-10th centile). The fever was 36˚C. His oropharyngeal examination was normal. His abdomen was soft. He had no dyspnea and auscultation revealed.

Table 1. The laboratory findings of the patient.

	Initial	at 2nd week
White blood cell count (4.5-10.5 109/L)	8.9	7.7
Neutrophil (1.78-5.38 109/L)	4.73	3.5
Lymphocyte (1.32-3.57 109/L)	2.98	4.2
Red blood cell count (4-6.2 1012/L)	4.94	4.8
Hemoglobin (110-166 g/L)	93	103.5
Platelet count (180-400 109/L)	454	376
MCV (75-90 fL)	68.6	67
RDW (11.2-15 %)	20	19
LDH (120-300 U/L)	242	218
ALT (0-40 U/L)	44	40
AST (0-41 U/L)	43	27
Ferritin (10.2-55.84 ng/mL)	161	120
Creatinine (0.26-0.77 mg/dL)	0.16	0.13
Total protein (57-80 g/L)	67.39	66
Albumin (35-52 g/L)	40.2	41
Prothrombin time (10-14 sec)	13	12
Activated partial thromboplastin time	35.2	30
Fibrinogen (2-4 g/dL)	1.73	1.96
D-dimer (0-500 µg/L)	1176	775
ESR (mm)	1/2	2/2
CRP (0-5 mg/L)	0.2	0.1
Troponin-I (<19.8 ng/L)	2.3	2.2
CK-MB (0.6-6.3 µg/L)	1.1	1.18

Nasopharyngeal swabs were obtained for the detection of SARS-CoV-2 RNA. The laboratory examinations revealed positive reverse real-time polymerase chain reaction (rRT-PCR) for SARS-CoV-2. The complete blood count revealed low hemoglobin (Hb), low mean corpuscular volume (MCV), elevated red cell distribution width (RDW), and increased platelet count. Biochemical parameters were within normal limits except for decreased creatinine, increased ferritin, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels. Coagulation tests were within normal limits. D-dimer was elevated. The laboratory findings are shown in Table 1.

Computed tomography (CT) of the chest revealed increased emphysematous aeration in both lungs, accompanying sequelae fibrotic densities, and band-style atelectatic areas. The patient was out of follow-up for the last two years and thus could not take ERT. Due to lack of treatment, lungs were affected, and these CT findings were attributed to GD itself not SARS-CoV-2 infection.

ERT was not delayed. In the observation period after ERT, no clinical decompensation was observed. Second rRT-PCR for SARS-CoV-2 from nasopharyngeal swabs in the second week was negative. D-dimer decreased. The patient was asymptomatic and no change was detected in his physical examination. Written informed consent was taken.

Discussion

The standardized birth incidence of GD in the general population varied from 0.39 to 5.80 per 100 000, and the prevalence ranged from 0.70 to 1.75 per 100 000, higher among the Ashkenazi Jewish population [4], and 2.3/1000000 in our country [5]. The most common type of GD, type 1 is characterized by hepatomegaly, splenomegaly, anemia, thrombocytopenia and bone involvement. Treatment consists of intravenous ERT (imiglucerase, velaglucerase, or taliglucerase) and oral inhibitors of glucosylceramide biosynthesis (miglustat or eliglustat) [1]. Our patient had dispnea, hepatosplenomegaly and bicytopenia on admission in 2013. Examinations revealed Gaucher cells in bone marrow aspiration and deficient beta-glucosidase enzyme activity in leukocytes (200-2000pmolspot.20h- Hamburg University Medical Center). He had homozygous c. 1448T>C (rs421016) (p.L483P) mutation. He was started on (60 U/kg/2 weeks) ERT.

Patients with several rare metabolic and genetic diseases are likely to be at risk of life-threatening acute metabolic decompensation and severe clinical course in case of SARS-CoV-2 infection [6]. It has been proposed that both GD and SARS-CoV-2 appear to be characterized by lysosomal involvement or disruption, and both share the central role of proinflammatory responses, triggering autoinflammatory cascades involving a wide spectrum of myeloid cells, cytokine/chemokine secretion and NLRP3 inflammasome activation, and elevation of cytokines (IL-2R, IL-6, IL-10, MIP1-α and TNF-α) [7].

Mistry et al. [7] recommended that ERT should be continued without prolonged interruption, which could trigger hyperinflammation and potentially exacerbate the severity of SARS-CoV-2 infection. ERT was postponed only 3 days in our patient. In the observation period after ERT, no clinical decompensation and worsening of laboratory parameters were

observed.

A link has been reported between SARS-CoV-2 and pediatric multi-system inflammatory syndrome disease causing cardiogenic or vasogenic shock requiring intensive care, and it is not yet established whether patients with GD have a risk of severe SARS-CoV-2 infection.

Conclusion

Physicians should consider these patients at risk and be alert about early testing and diagnosis. Although a definite interpretation can not be made with a single case, we think that ERT should not be interrupted, with close follow-up in order not to disrupt treatment of disease.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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How to cite this article:

Nafiye Urgancı, Nazan Dalgıc, Dilek Guller, Merve Usta. *Gaucher disease and SARS-CoV-2 infection: A case report. Ann Clin Anal Med 2023;14(Suppl 2):S200-202*